

# THE CANCER LETTER

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## CMS Opens Door to Coverage Of Comprehensive Genomic Sequencing

*By Paul Goldberg*

At first glance, it's hard to imagine anything as obscure as a policy by a private contracting firm that runs the Medicare program in the Carolinas, Virginia and West Virginia.

But look closer: a "local coverage determination" by Palmetto GBA addresses an urgent, vexing problem of precision oncology: how advanced molecular testing can be used to determine treatment options for individual patients and what insurers will be willing to pay for.

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## Duke's Legal Stance: We Did No Harm

*By Paul Goldberg*

Attorneys defending Duke University are preparing to argue that no patients were harmed in the institution's phase II clinical trials of genomic predictors that were later shown fraudulent.

The technology in question came from the laboratories of Duke stars Joseph Nevins and Anil Potti, and was based on findings that, from the outset, seemed too good to be true—and were ultimately discredited and retracted.

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### News Analysis

## Misconduct Expert Dissects Duke Scandal

*By C. K. Gunsalus*

On Jan. 9, 2015, The Cancer Letter reported that Duke University received information in early 2008 that called into question the validity of the methodology and results published by the Anil Potti research group. Potti, along with his mentor and co-author Joseph Nevins, had galvanized the world of cancer research in 2006 and 2007 with their reports of successful gene expression tests for directing cancer therapy, the "holy grail" of cancer

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## CMS Publishes Groundbreaking Determination with no Rollout

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The coverage determination, titled “Comprehensive Genomic Profiling for Non-Small Cell Lung Cancer” popped up on a government website well after close of business Jan. 22. There was no press release; no rollout whatsoever.

Nonetheless, the decision may introduce clarity into the informational pea-soup fog that engulfs molecular testing by spelling out the criteria for opening payment for complex tests and comprehensive genomic assays, which measure multiple markers.

As it stands, the vast majority of assays that cost thousands of dollars and are used to determine treatment for cancer patients are not reviewed by government agencies before they enter the marketplace.

Moreover, Medicare claim forms make it impossible for nearly all payers to determine what the tests are for and how effective they are (The Cancer Letter, [Aug. 8, 2014](#)). With more than 11,000 laboratories selling tests that fit under a small number of codes, Medicare administrators and private insurers typically get claims for they-don't-know-what. And they pay at least some portion of those claims.

Palmetto's [new policy](#) is poised to determine how coverage decisions will be made regarding laboratory-developed tests that involve a type of sequencing-based genetic profiling. The policy may also harmonize coverage decisions made by CMS with validation of assays by FDA and New York State, which has long been held as the reference standard for LDT's validity (The Cancer Letter, [Oct. 3, 2014](#)).

**Editor & Publisher:** Paul Goldberg

**Associate Editor:** Conor Hale

**Reporter:** Matthew Bin Han Ong

Editorial, Subscriptions and Customer Service:

202-362-1809 Fax: 202-379-1787

PO Box 9905, Washington DC 20016

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How accurate are the results of unregulated laboratory-developed tests?

Ideally, the LCD will clarify vexing clinical dilemma that occur every day in the oncologists' offices.

For example, what course of treatment would you propose to a patient diagnosed with metastatic non-small cell lung cancer who is a lifetime non-smoker with no toxic exposures whatsoever? According to guidelines and good practice, the patient's tumor specimen should be sent out for testing for both EML4-ALK translocations and EGFR mutations.

Without stringent regulation of such tests, the physician cannot be certain whether the results are reliable.

This is a life-and-death question, because the presence of these markers makes it possible for the patient to be treated with targeted drugs, often with outcomes far exceeding those of cytotoxic chemotherapy, the de facto alternative in most cases.

A false-negative finding would deprive the patient of these options.

The Palmetto decision focuses on coverage of somatic comprehensive genomic profiling (S-CGP) for patients with metastatic non-small cell lung cancer, limiting testing to those who are lifetime non-smokers or former light smokers (with less than or equal to a 15 pack-year history) and who have tested negative for epidermal growth factor receptor mutations and EML4-ALK rearrangements when initial testing was done by an FDA-approved companion diagnostic or by a laboratory developed test for these mutations.

S-CGP, if positive, may allow patients to be treated with a targeted therapy for which they were previously ineligible, the coverage decision suggests.

The policy is particularly important because Palmetto's experiment may presage the Centers for Medicare and Medicaid Services strategy for making sense of the many laboratory-developed molecular tests and defining their place in what is called personalized medicine.

A new law, [the Protecting Access to Medicare Act of 2014](#), validates the work began by Palmetto, in as much as it allows Medicare to defer to the expertise of one or more contractors to either “establish coverage policies or establish coverage policies and process claims for payment for clinical laboratory tests.” Under the act, Palmetto may become an authority for determining which tests are paid for system-wide.

Over the past three years, Palmetto's program, [called MolDX](#), headed by Elaine Jeter, has been working to identify tests, establish what they are able to detect, assess their usefulness, and establish coverage.

Palmetto uses unique identifiers that make it possible to identify molecular tests and their purveyors. No other Medicare contractor has an analogous program.

And since Palmetto knows what it pays for, it can set policies and refine them.

For now, the Palmetto LCD is binding only in the company's territories and not for Medicare as a whole; however, this could eventually become Medicare policy.

"The Palmetto LCD is potentially transformative for two reasons," said Vincent Miller, chief medical officer of Foundation Medicine Inc., a company that provides comprehensive profiling. "First, this LCD recognizes the fundamental distinction between a comprehensive genomic profile, such as FoundationOne, and hotspot genes or panels of multiple genes that focus primarily on specific base pair substitutions only.

"Second, this LCD highlights the critical importance of rigorous analytic validation of comprehensive genomic profiles. While starting in a subset of non-small cell lung cancer, the leading cancer killer of men and women in the U.S., this LCD should pave the way for coverage and value-based payment of comprehensive genomic profiling in additional indications."

Foundation Medicine, which has published validation data for its tests, is likely to be the first company to benefit from the LCD. The list price of the FoundationOne assay is \$5,800.

Earlier this month, pharmaceutical giant Roche acquired a majority interest in Foundation Medicine, offering to purchase up to 56.3 percent on a fully diluted basis through a tender and acquisition of newly issued shares. Roche will tender for approximately 15.6 million Foundation Medicine shares at \$50 per share with an aggregate tender value of approximately \$780 million. The transaction is expected to close in the second quarter of 2015. Roche will also invest \$250 million in Foundation Medicine by acquiring 5 million newly issued shares at \$50 per share.

Memorial Sloan Kettering Cancer Center also has a comprehensive genomic profiling technology, called MSK-IMPACT.

Another company that stands to benefit is Illumina Inc., which sells the underlying sequencing technology.

One other potential player, CARIS Life Sciences (The Cancer Letter, [Aug. 8, 2014](#)) will likely be shut out, since its Next Gen Sequencing approach doesn't cover all the types of alterations that the Palmetto memo requires of an approved test.

None of these companies have sought technical evaluation through the Palmetto MolDx program for this indication at this writing.

Palmetto's objective is to understand the robustness of the initial testing methodology in patients that are subsequently found to harbor mutations found by CGP. Though it's impossible to predict where the science will go, it is almost certain that this clinical introduction will be the first of many dealing with advanced omic tests that will be introduced as the clinical data matures and is continually broadened.

Overall, the move toward newer, more comprehensive sequencing technologies makes sense to drug developers and regulators.

Multiplexed or multi-analyte tests are more efficient, experts say. "In situations where you have a limited amount of tissue and separate tests for each of several possible markers, you may run out of tissue before all the tests can be done," said Mace Rothenberg, senior vice president and chief medical officer at Pfizer Oncology. "So having one test that can evaluate several markers simultaneously is very appealing. Like any test that is intended to be used as a companion diagnostic, the results need to reliably identify underlying molecular or genomic characteristics that make that an individual's tumor appropriate—or inappropriate—for treatment with a particular therapy."

For years, pharma companies have been petitioning FDA to step in and start regulating laboratory-developed tests, and now the agency is preparing to do so, starting [with tests in high-risk diseases](#).

FDA has approved three companion diagnostics for drugs intended to treat non-small cell lung cancer. Such tests look at specific sequences in the target gene to determine if a mutation is present.

For the EGFR mutation, the agency has approved the Cobas EGFR Mutation Test for erlotinib. Also approved is Therascreen EGFR RCQ PCR Kit for afatinib. For the ALK mutation, the agency has approved the Vysis ALK Break Apart FISH Probe Kit, intended to be used with crizotinib.

But the FDA has also approved many targeted oncology drugs without assigning a specific companion diagnostic alongside. This is true for the approval of Genentech's Herceptin (trastuzumab), which is only covered with Her-2 testing, and Novartis' Zykadia (ceritinib), a follow-on drug to Pfizer's Xalkori (crizotinib) for the ALK rearrangement.

There are many other ways to identify these mutations. These include PCR, bidirectional Sanger sequencing, direct DNA sequencing, hybridization sequencing, pyrosequencing and sequencing by denaturation. Alas, no data exist to enable comparisons of diagnostic accuracy of these technologies.



Deleterious EGFR and ALK mutations may be missed by CDx or LDT sequencing techniques because either the mutations occur outside the defined analytic framework of the gene or there are complex mutations, including insertions or deletions (indels), duplications (dups), or translocations that often are not found by traditional methods.

By contrast, massively parallel sequencing (also known as next generation sequencing, or NGS), of which CGP is a specific subtype, can offer increased sensitivity, because it can analyze the entire coding region of a gene, identifying mutations CDx and LDT technologies can't see.

A recent study cited in the LCD by Palmetto, led by Alexander Drilon of Memorial Sloan Kettering Cancer Center, raises questions about the adequacy of some laboratory-developed tests. The paper was published online Jan. 7 [in the journal Clinical Cancer Research](#). The findings were previously presented at the [2014 ASCO annual meeting](#).

*The text of the LCD follows:*

#### **Coverage Indications, Limitations, and/or Medical Necessity**

This policy provides limited coverage for comprehensive somatic genomic profiling (hereafter called CGP) for patients with metastatic non-small cell lung cancer (NSCLC) who are lifetime non-smokers (also known as never-smokers) or former light smokers ( $\leq 15$  pack year history) **and** who tested negative for epidermal growth factor receptor (EGFR) mutations and EML4-ALK translocations when initial testing was done by an FDA-approved companion diagnostic (CDx) or by a laboratory developed test (LDT) for these genomic alterations. Alterations detected by CGP, if positive, may allow individuals to be treated with a targeted therapy for which they were previously ineligible. At the current time, CGP for germline (i.e. inheritable) mutations is not a Medicare benefit.

#### **Background**

It is estimated that more than 220,000 new cases of lung cancer will be diagnosed in the United States (US) this year. This represents roughly 13% of all new cancer diagnoses, and 27% of cancer deaths. Sadly, the estimated 5-year survival rate for all lung cancer patients is 17%, and only 4% for patients with metastatic disease.

The pathophysiological development of lung cancer is complicated, with several known genomic alterations found individually or in combination in many patients. These alterations may be due to toxic

exposure or underlying genetic factors, and not all alterations have the same impact on disease development or prognosis. Some alterations appear to be integral to the transformation and ongoing growth of the tumor (driver mutations). Among the best studied in this class are point alterations and indels in EGFR and EML4-ALK translocations. EGFR mutated NSCLC is found in up to 15% of all lung cancers in the US. These mutations convey a more favorable prognosis and allow treatment with oral EGFR inhibitors such as erlotinib, gefitinib, or afatinib. Similarly, translocations of ALK and EML4 or other less common fusion partners occur in approximately 4% of all NSCLC patients and permit treatment with oral ALK-targeted inhibitors such as crizotinib and ceritinib.

The majority of NSCLC cases are diagnosed in patients with a smoking history. Lifetime non-smokers or light former smokers ( $\leq 15$  pack years) have different disease compared to their heavier smoking counterparts. Sequencing of tumor specimens in never-smokers has shown a higher mutation frequency of EGFR than smokers, with some non-smoking ethnic groups such as Asian women having a much higher mutation frequency than their Caucasian counterparts. Similar results have been shown with ALK translocations. For example, in one study involving never-smokers or light smokers with adenocarcinoma of the lung, 22% of patients' tumors harbored an ALK. When EGFR mutation carriers were excluded, 33% of patients had an ALK translocations. While ALK translocations and EGFR mutations certainly occur at a meaningful frequency in former smokers with more significant history of cigarette use, use of the enrichment approach described herein may allow a more efficient completion of this initial phase of study.

Currently, a variety of different techniques are used to test for these genomic alterations in tumor specimens including three FDA cleared/approved CDx tests for NSCLC to determine if a patient is a candidate for targeted therapy. For EGFR, there is the Cobas® EGFR Mutation Test for erlotinib and Therascreen EGFR RCQ PCR Kit for afatinib. For ALK, there is the Vysis ALK Break Apart FISH Probe Kit for crizotinib. These tests look at specific regions in the target gene to determine if the genomic alteration of interest is present.

In addition to these FDA-approved CDx test, there are a variety of laboratory-developed tests (LDTs) that are used to identify EGFR mutations and ALK translocations. These include bidirectional Sanger sequencing, direct DNA sequencing, hybridization sequencing, pyrosequencing and sequencing by

denaturation to name a few. Some of these LDTs provide more extensive genetic analysis than their FDA-approved counterparts, but there are few head-to-head comparison studies demonstrating greater diagnostic accuracy or clinical utility of the various approaches.

For various reasons, CDx or LDT sequencing techniques may miss deleterious EGFR mutations and ALK translocations. For example, alterations may occur outside the sequenced region or involve complex alterations (e.g. insertions or deletions (indels), copy number alterations, or translocations) that are not detectable by the specific test. Newer techniques such as massively parallel sequencing, also known as next generation sequencing (NGS), offer the possibility of not only increased analytical sensitivity but also the ability to detect a broader range of genomic alterations than existing CDx and LDT techniques.

In a recent study by Drilon, lifetime non-smokers or light smokers who tested negative for alterations in various target genes (including EGFR and ALK) in a broad “focused panel of a variety of non-NGS” tests developed at a major academic institution were studied using a specific type of NGS, namely CGP. Despite robust non-NGS (and CGP) testing using multiple techniques, CGP testing identified EGFR mutations in 7% more patients than had been identified by prior combined methodologies, and 6% more ALK translocations than by previous FISH analysis. Although some of the EGFR mutated malignancies found by NGS are less likely to respond to available EGFR tyrosine kinase inhibitors (TKIs) (e.g. exon 20 insertions), others such as complex double mutations and exon 18 mutations (which are typically undetectable with so-called “hotspot” panels), are likely to benefit from targeted therapy. CGP analysis was equally compelling for ALK translocations. In two patients, where FISH analysis was clearly negative, translocations were identified using CGP. These patients would likely benefit from treatment with crizotinib.

Although the study population is small, the significant number of potentially actionable genomic alterations that were missed by non-NGS methodologies is compelling, and demonstrates that CGP can identify a group of non-small cell lung cancer patients who are likely to benefit from targeted therapy.

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## **Comprehensive Genomic Profiling (CGP) Test Description:**

CGP analysis is defined as a single test that does not distinguish between somatic and germline alterations and can detect the following classes of alterations:

1. Base pair substitutions (including single nucleotide variants (SNVs))
2. Insertions and deletions (Indels; up to 30-40 bp)
3. Copy number variations (CNVs; ploidy < 4 with copy number ≥ 8)
4. Translocations

Other non-NGS testing platforms may be considered as long as they can similarly detect all four classes of alterations with comparable test performance as CGP.

## **Test Performance**

The analytical performance of CGP has been assessed in a validation study by Frampton. Similar testing performance is noted in the Drilon study. These assays demonstrated analytical sensitivity of 95-99% across the four classes of genomic alterations and analytical specificity reported as a positive predictive value of > 99%. In addition, inter-batch precision was 96.4%.

## **MolDX CGP Analysis Coverage**

CGP analysis is covered only when the following conditions are met:

- Patient has been diagnosed with advanced (Stage IIIB or IV) NSCLC, **and**
- Patient is a lifetime non-smoker or former light smoker with ≤15 pack year history of smoking, **and**
- Patient previously tested negative for EGFR and/or ALK translocations through non-CGP methods, **and**
- Testing is performed by a lab that has been verified by MolDx to demonstrate analytic sensitivity, specificity and reliability comparable to the CGP studies noted in this policy. Those labs whose testing is verified to be comparable will be notified in writing and posted on the MolDX website, **and**
- Palmetto GBA expects participating laboratories to:
  - Prior to CGP testing, verify that each patient has previously tested negative for EGFR and ALK translocations **and**,
  - Identify the specific non-CGP methodology used for any patient when an EGFR and/or ALK translocations is identified by CGP, **and**
  - Report the following to MolDX every six months:
    - Number of patients tested;
    - Total number of patients with no EGFR/ALK translocations by CGP;
    - Number of patients with EGFR/ALK

translocations by CGP whose mutations were not identified by non-CGP methods. Report on whether the mutation(s) occurred outside the defined analytic framework of the genes identified by the respective CDx and whether the mutations are attributed to insertions or deletions (indels), duplications (dups), or translocations.

- For each identified EGFR/ALK translocation by CGP, the response status and duration of response;
- At the discretion of a lab, other mutations that are identified.
- Reports will be delivered in every 6 months in a mutually acceptable format, **and**
- Submit reports according to HIPAA standards.

## Patients Received Standard Care, Not Harm, Duke Argues

(Continued from page 1)

[The suit](#) claims negligence, breach of fiduciary duty, unjust enrichment, infliction of emotional distress, loss of chance, battery, deceptive trade practices, civil conspiracy and obstruction of justice.

The trial is scheduled to begin Jan. 26 at Durham County Superior Court. Altogether, 117 patients enrolled in the three clinical studies at Duke.

The essence of Duke's argument—which forms the basis of a flurry of motions for a partial summary judgment—is that patients who entered the clinical studies were, for the most part, in late stages of disease and that the predictor models were used to assign them to existing therapies.

The plaintiffs' attorneys argue that Duke had ample opportunities to recognize that the technology tested in the three trials was fraudulent. Instead, in the spring of 2008, Duke officials [silenced a whistleblower](#), [frustrated an NCI inquiry](#), and, in the fall of 2009, [set up a biased internal review of the three trials](#).

On top of that, the deans who were directly involved in silencing the whistleblower later told a committee of the Institute of Medicine that no whistleblower had come forward from Potti's lab.

These signals—had they been taken seriously—could have led Duke to stop the three clinical experiments it was conducting.

The consent forms signed by the patients who enrolled in the studies extolled the potential of Duke's technology.

This genomic predictor looks at hundreds of genes (pieces of DNA—a short form of deoxyribonucleic acid that contains information needed to construct and operate the human body) in your tumor. In initial studies,

the genomic predictor seemed to determine which drug would be effective in a given patient with an accuracy of approximately 80%. The genomic predictor is still being tested in research studies and is therefore considered investigational."

As the case moves to the courtroom, it will demonstrate how the fundamentals of medical ethics translate into the context of legal disputes.

"There is no question that serious ethical lapses occurred," said Wylie Burke, professor in the Department of Bioethics and Humanities and adjunct professor in the Department of Medicine (Medical Genetics) at the University of Washington.

"The first set of lapses related to Potti's research misconduct. He evidently either fabricated or manipulated data to support the validity of the genomic predictor test that was presented as a scientific breakthrough and then used in clinical trials.

"Were others implicated in this misconduct? It is hard to know, but certainly there was a failure of effective research participation on the part of his collaborators. At best, the sequence of events illustrates the willingness of others on the scientific team to accept Potti's results without questioning or even fully understanding them; at worst, others may have been complicit in the misconduct.

"The second set of lapses was the failure on the part of several people at Duke to take concerns about Potti's research seriously," said Burke, who was asked by The Cancer Letter to review several court filings. "The unwillingness to respond effectively to Perez's concerns might be a symptom of the hierarchical bias often seen in academic institutions: the word of a lowly medical student (even an obviously talented one, who has carefully substantiated his concerns) tends to carry much less weight than that of a professor (problem in itself).

"At the very minimum, however, Nevins should have followed up on Perez's concerns with an independent look at the data, if only (in his own mind) to assure himself that all was well. The concerns expressed by [MD Anderson Cancer Center statistician Keith] Baggerly [who led an independent investigation of the Duke results] and colleagues should also have led to re-evaluation of the data. Much would have turned out differently if Nevins had done so, and his failure on this point remains incomprehensible.

"The third set of lapses was the cover-up," Burke said. "It is difficult to escape the impression that at a certain point officials at Duke decided to circle the wagons and deny knowledge of events (such as Perez's communication of concerns) in order to limit damage to

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## A modest proposal for the Duke gift shop.

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the institution. That they did so through several stages of investigation, including in testimony to an IOM committee, is deeply troubling.

"I defer to legal experts on the implications from the perspective of the law. It is probably accurate to say that the patients enrolled in the trials were by and large not harmed by their participation, in the sense that their life expectancy was likely not changed. Yet the claim that patient's quality of life was harmed by decisions she made based on Potti's false assertions must be taken seriously.

"And there are harms that are not effectively addressed by the courts. It is a harm to be lied to; it is a harm to be given false hope. The harm is first and foremost to the research participants, but it is also a harm to the research enterprise itself."

### No Harm Done?

Duke's motions for a summary judgment argue that the case should turn on North Carolina law, as opposed to established ethical constructs.

In an effort to determine the burden of proof that has to be met by the plaintiff to demonstrate negligence per se, Duke's motion states that standards contained in the 1979 report by the National Commission for protection of human Services of Biomedical and Behavioral Research, known as [the Belmont Report](#), don't create obligations under North Carolina law. Similarly, they argue that the federal law, Title 45 part 46 [of the Code of Federal Regulations](#), which sets out

requirements for research institutions, is not a part of North Carolina law, either.

Duke basically states that it did nothing wrong.

"Plaintiffs cannot show that a different course of treatment would have made any difference in their care or chance of survival," the Duke motion reads. "Expert testimony in this case has not established that any clinical trial available in the United States in 2010 would have prolonged plaintiffs' life expectancy or treated them more effectively. Therefore, plaintiffs cannot meet causation of damage elements of their negligence per se claim."

Another court filing deals specifically with the case of Juliet Jacobs, a patient with metastatic lung cancer who—with Potti's knowledge—made a recording of the now disgraced doctor as he presented the trial to her. Juliet's widower, Walter, is one of the plaintiffs.

Duke attorneys argue that in that specific instance, "these defendants did not abuse, breach, or take advantage of Mrs. Jacobs's confidence or trust. Instead, they were open, fair, and honest with Mrs. Jacobs and her husband regarding her prognosis and treatment options. Mr. & Mrs. Jacobs were made aware that the clinical trial may increase, decrease or have no effect on Mrs. Jacobs's likelihood of responding to chemotherapy. They were also encouraged to seek other treatment alternatives."

Duke's filings also hold that "the undisputed evidence in this case has established that there was no clinical trial or other treatment available in the United



States in 2010 that would have cured Mrs. Jacobs's cancer or prolonged her life expectancy. Plaintiff cannot show that a different course of treatment would have made any difference in Mrs. Jacobs's chance of survival."

Duke attorneys are not representing Potti, who was dismissed from the university. However, they are representing Nevins, the deans, the IRB chair and the spinoff company that was going to commercialize the Nevins-and-Potti inventions.

The defendants argue that the plaintiffs cannot prove "negligence per se" claims because they cannot show that there was "(1) a duty created by a statute or ordinance; (2) that the statute or ordinance was enacted to protect a class of persons which includes the plaintiff; (3) a breach of the statutory duty; (4) that the injury sustained was suffered by an interest which the statute protected; (5) that the injury was of the nature contemplated in the statute; and (6) that the violation of the statute proximately caused the injury."

Plaintiffs argue that Duke is ultimately responsible for the actions of its scientists and administrators.

"Defendants admit that Dr. Potti fabricated, falsified and intentionally manipulated the data that formed the 'basis for clinical trials' in which Juliet Jacobs was enrolled," one of the plaintiffs' filings states. "Much of the... falsified, fabricated, and manipulated data came from the laboratory of Dr. Nevins, for which he was ultimately responsible. In fact, Dr. Nevins admitted one set of 'intentionally altered' data that came from his lab 'provided support for the lung cancer trials...'

"Manipulating and fabricating the data for a clinical trial and then lying to a patient to obtain informed consent is a breach of good faith. It constitutes battery and invalidates informed consent. Dr. Potti is the physician who presented the informed consent to the plaintiffs. He is the one who falsified, fabricated and intentionally manipulated the data. He entered into a Consent Order with the North Carolina Medical Board admitting that he committed 'unprofessional conduct.' He admitted that there was a responsibility to tell the patients, including Juliet Jacobs, about the controversy with the medicine. Dr. Potti did not inform the Jacobs of either the 'controversy' or the fraud."

Nevins acknowledges that he did not examine the data until October 2010, three months after this publication reported that Potti had misstated his credentials, claiming to have been a Rhodes Scholar, and after Potti was barred from Duke campus.

### **"Money, Fame and Overall Fortune"**

Countering Duke's assertion that no one was injured because patients were assigned to standard therapy, the plaintiffs say that Juliet Jacobs was falsely led to accept a treatment regimen she would not have ordinarily considered.

The patient's husband and daughter "testified to the exact opposite," the filing reads. "Plaintiffs showed that Juliet and Walter Jacobs did not want standard of care chemotherapy and would not have participated if it had not been for the defendants' fraud."

The Duke protocol required a second biopsy and led the patient to a chemotherapy regimen that was more aggressive than she would have ordinarily chosen for end-of-life care.

"The second biopsy was not required for the alleged 'standard of care' chemotherapy—it was required for participation in the clinical trials," the plaintiffs argue. "Defendants want to turn a lawsuit based upon personal injury into a wrongful death action. The question is not whether 'standard of care chemotherapy' was provided and whether or not the same caused her death. Instead, the question posed by the plaintiffs is whether or not the defendants' actions caused a personal injury to Juliet and Walter Jacobs. Attempting to recast this as a wrongful death action... is a red herring thrown to distract the finder of fact."

Most importantly, Juliet Jacobs was deceived, the plaintiffs' attorneys argue.

"Because her quality of life was very important to her, if she had been given proper consent and told that there was no 'silver bullet' and if she had not been told by Dr. Potti that he could give her a chance to live for ten years, she and Walter would more likely than not have made other choices regarding how they spent her last days and what quality that life would have."

An audio recording of the Jacobs meeting with Potti captures the doctors expressing hope for a miracle.

In the recording, Juliet Jacobs says that her son-in-law has had chemotherapy for a decade, and that he is the only survivor in a clinical trial.

Potti: "Wow. And I, I wouldn't be surprised if I expect that from you. That's what I mean. I'm 100 percent on board here, OK?"

Like other patients, Jacobs was presented with a consent form that contained the claim that the genomic predictor that would be used had the accuracy of approximately 80 percent.

Instead of going into hospice care, Juliet Jacobs ended up with a lot of toxicity and a quality of life her family members described as poor.



The date of the family's meeting with Potti is important: Feb. 11, 2010, a month after Duke restarted the trials following an internal investigation that has since been shown to be cursory and skewed. That controversy was never mentioned to the prospective patient and her family.

Knowing what he knows now, Walter Jacobs is furious.

"I know that it's an immoral, evil, awful thing that has been done," he said in a deposition.

The plaintiffs also allege a "civil conspiracy."

"The underlying conspiracy was among the defendants and Dr. Potti and Dr. Nevins, on behalf of themselves and on behalf of their outside financial interest, Cancer Guide, to cover up the falsification in order to continue the clinical trials. The successful conclusion of the clinical trials would have meant money, fame and overall fortune."

### News Analysis

## **Gunsalus: Duke Administrators Deferred to a Luminary**

(Continued from page 1)

research. The 2008 information came in the form of a letter from a third-year medical student, Brad Perez, who was working in Potti's lab. The letter, which does not seem to have been given any credence at the time, described with precision the problems that eventually resulted in the termination of clinical trials and the subsequent retractions, beginning in 2011, of at least ten (and counting) papers from major scientific journals.

We know that his letter was read by Potti, Nevins, and various high-level administrators at Duke (1).

We don't know what those Duke administrators were thinking when they read the cogent and careful summary of "[Research Concerns](#)" that Perez had developed about the validity of the high-profile research in which he was participating, and with which he had made himself deeply familiar. Perez made it clear that his reservations were so serious that he was knowingly jeopardizing his career by taking the extraordinary steps of challenging his boss, leaving the Potti laboratory early, and removing his name from four papers destined for prestigious journals. Indeed, in his measured words, he chose to repeat an entire year of his medical education to replace his time in the Potti lab with "a more meaningful" research experience.

We do know that the concerns expressed by Perez, which only very recently became public

knowledge, were not the only ones known to the Duke administration in 2008. By the time Perez raised his concerns, the MD Anderson biostatisticians Keith Baggerly and Kevin Coombes had been trying and failing to replicate the research methods. We know this led them to seek information about, and then question the methods and data in the Potti/Nevins papers from shortly after the first reports of successful genomic predictors were published.

We do know that Duke referred Perez to Potti's boss, Dr. Nevins, to discuss his concerns. We know that, at the time, Nevins was deeply invested in the success of Potti's research through co-authorship, co-inventorship, and his status as co-founder of the company built around it.

We know that, after meeting with Nevins, Perez acceded to what he understood to be advice not to share his concerns with his funding source, the Howard Hughes Medical Institute, and that he did so because he trusted Dr. Nevins to review the research in light of his concerns. We know that no one at Duke looked at the data or the methods Perez questioned.

We know that Nevins, who promised to and then did not examine the data, testified that, in his eventual 2010 review, it took him less than an hour to find "[abundantly clear](#)" manipulations in the data. It appears that Nevins only looked at the data after it was revealed that Potti was not the Rhodes Scholar he had claimed to be on his CV and in federal grant applications.

We know that the same research was the basis for clinical trials began in 2007 and eventually enrolled more than 100 patients, all of whom were seriously ill with advanced cancer. We know the informed consent documents signed by the patients described the trial in this way:

"The purpose of this study is to evaluate a new tool, a genomic predictor...In initial studies, the genomic predictor seemed to determine which drug would be effective in a given patient with an accuracy of approximately 80%."

We know that the results did not have an accuracy of 80 percent, because the research was error-ridden and manipulated.

We know that clinical trials were, in the words of a Duke administrator, were based on a theory that was "[a dud](#)." Given what is known about the research, the trials should never have been run.

We know that this state of affairs persisted from early 2008 to late 2010, when the clinical trials were finally terminated. Achieving that outcome took extraordinary persistence by Drs. Baggerly and

Coombes, concerns expressed by the National Cancer Institute, an unprecedented letter signed by more than 30 prominent statisticians expert in this area, the indefatigable coverage of The Cancer Letter, the revelation of a fudged CV, and unrelenting publicity.

We know that when the Potti lab's research was later the subject of multiple investigations, Duke administrators didn't reveal the Perez letter. They didn't share it when a clinical trial based on the research was suspended in 2008 while external statisticians reviewed the methodology. They didn't report it to the National Cancer Institute. They didn't provide it to the Institute of Medicine Translational Omics review committee. They [testified](#) to investigators that Duke had not had any whistleblower reports (p. 257), and that "[in no instance](#) did [any co-authors] make any inquiries or call for retractions until contacted by Duke." (p. 251)

Of course, by the time they were asking, Perez had withdrawn his name and was no longer a co-author.

Is this really how it is supposed to work? Should detecting and stopping bad and harmful research be this hard? Even when the research provides a beguiling and well-funded vision of possibilities? When even its critics would like to find it valid?

### **How Does This Happen?**

In 1993, Drummond Rennie and I wrote that the modern era of what we now call scientific misconduct dates to 1974. (2) By 1993, a fair amount was known about how to build institutional structures to promote research integrity. I wrote a summary that year in *Academic Medicine*, a portion of which reads: "institutions must establish a misconduct review process that can render objective, fact-based decisions untainted by personal bias and conflicts of interests. In developing such a process, leaders must be aware of probable pitfalls, establish an accessible structure, and provide for consistent assessment of allegations and complaints, focusing on facts, not personalities." (3)

As this situation shows, almost two decades on, even a research powerhouse like Duke can struggle with these fundamentals. Responding to allegations of misconduct by members of one's own institution is hard. (It's harder to go in and investigate effectively as an outsider, though both can and must be done at times.) There are far more ways to go wrong than you might imagine, especially when experience shows that most concerns expressed turn out not to have any factual basis, but to be rooted in personality conflicts, misunderstandings, and other unhappiness. In a career as a university administrator—

in research administration and in a provost's office handling problems, conducting internal investigations, developing policy, and ultimately focusing on training for preventing problems—I made many mistakes and I have observed other well-meaning, earnest, and honorable people make mistakes. My starting assumption is that the actions of Duke's administrators were just as well-meaning and well-intended. At the same time, we have by now accumulated a considerable body of knowledge about the cognitive errors and procedural shortcomings that can infect these situations, and it is time for us as a community to begin to heed and apply those lessons.

The failings in this matter are not unique to Duke. They are not new. They map closely to other failings that have been seen repeatedly over many years at high-powered, well-funded, sophisticated research institutions. Whether the result of the cognitive biases to which we are all susceptible (confirmation bias, egocentrism, gain-loss aversion, self-deception, etc.), the incentives and pressures of today's biomedical research system, (4) the exceedingly short half-life of institutional memory and experience, or motivated blindness, (5) the consequences are severe and impose great costs upon many.

The integrity of institutions is rooted in individual actions that must be supported and reinforced. It takes constant effort to encourage people to do the right thing for the right reasons in the face of temptations, distractions, and money. One mechanism for achieving that is to focus on inculcating an [integrity mindset](#) that finds ways to prompt and remind those faced with fighting fires of the larger stakes. Immediacy and promise can, and often do, subvert long-term institutional best interests. Exploring how this pattern repeats itself can help us understand how this could have happened. Let's start with three glaring examples illustrated here that recur in practically every botched research misconduct investigation: fundamental mischaracterizations of matters in front of one's face, excessive deference, and conflicts of interest.

### **1. Mischaracterizing the Situation**

There are two key junctures here where the consequences of mischaracterization are particularly painful. First, Duke officials have emphasized throughout this sad affair that top-notch clinical treatment was provided the trial patients. This misses the point. An emphasis on treatment minimizes and diverts attention from the profound breach of responsible conduct of the research that is the *raison*

d'être of a research institution. Second, they seem to have categorized the 2008 letter from Perez along the lines of “differences of opinion among researchers posed by junior member of team,” or, “student doesn't get it, needs to be referred back to supervisory chain,” instead of as one raising important red flags about the integrity of research.

Let's look at the effects of each of these mischaracterizations.

### **A. Mischaracterizing the Situation: Clinical Treatment vs. Research Integrity**

In the “[Deception at Duke](#)” 60 Minutes report in 2012, CBS quotes Duke's assurances that no one was really harmed, because all patients received the standard of care in chemotherapy. Yet patient treatment is not the primary goal of a clinical trial in which patients provide their informed consent for participating in research that is testing experimental interventions.

In the words of the survivors of some of the patients now suing Duke, the patients were seeking a chance at the “silver bullet” for survival, even with stage four cancer. (6) They were not asking “is this the best available treatment?” To be provided that was a given. They were asking “does this research give me—or someone else—a better chance than current treatments?” In their dire straits, they wanted the smartest doctors using the newest techniques based on the latest research.

The Duke clinical trials were using genomic predictors that were based on research at the Potti lab. In effect, the *test* was being tested. The patients were there because of the research. In consequence, the research misconduct is the key to what went wrong.

If you ask the wrong question, you are likely to get the wrong answer. The questions Duke's officials should have been asking were about their obligations to patients making themselves subjects for Duke's research, their obligations to the integrity of Duke's research mission, and their obligations to keeping the faith with their patients.

### **A Distressing Consequence: Duke's Legal Strategy**

Focusing on the standard of care treatments the patients received, Duke is taking an aggressive legal posture in lawsuits filed around the terminated clinical trials. While their filings are not specific administrators speaking directly, they are made on behalf of the institution and in Duke's name.

In essence, Duke's pending motions to dismiss

some of the claims against it argue that the patients would have died anyway, given their advanced cancers. This is at odds with the hopes provided by Dr. Potti and by Duke's advertisement with Anil Potti in it which starts: “Duke has made a commitment to fight this war against cancer at a [much higher level](#).”

Here are some direct quotes from Duke's legal filings: (7)

- patients received “standard-of-care therapy”;
- patients knew they were participating in a trial that might not have any benefit for them;
- Duke did not “abuse, breach or take advantage of [patients'] trust;”
- Duke did not “place Duke's interests ahead of” those of the plaintiffs,
- Duke's and patients' “interests were never in conflict”
- Duke was “open, fair and honest” regarding “prognosis and treatment options;”
- “plaintiffs cannot show that they were injured by any act or omission by Duke.”

In sum, Duke's legal position is that it cannot be shown that “a different course of action would have made any difference” in chances of survival.

Is that really the point?

Dr. Potti's separate legal team (he left Duke after the revelation about his CV falsification) takes a similar stance, that no different course of medical treatment would have affected the outcome. (That is, the same refrain that the patients would have died anyway.) Further, his team asserts that “Plaintiffs cannot establish that Dr. Potti committed professional negligence or that he benefited in any way from enrolling [name] in the trial.”

Put colloquially, “no harm, no foul”?

My litigator friends assure me that taking an aggressive legal posture to pare down charges and keep the most emotionally-laden aspects of the situation away from a jury is the legal equivalent of standard of care. If Duke's administrators are taking advice from their legal counsel, and their legal counsel is following the guidance of their external lawyers, one can see how they came to sign off on this defense: Duke does a lot of good for a lot of people and there's a lot of money at stake—and perhaps they already significant offers on the table in negotiations with the plaintiffs. Maybe they see this approach as protecting the institution of which they are stewards. But is it wise? Can it possibly be good for Duke? Can it be good for Duke patients?

The mismatch between scientific values and the rules of the road in the legal system, which are all too

often shown in cases involving scientific misconduct, is on full display here.

How will this strategy affect those who rely on public trust to enroll patients in clinical trials? Is this approach healthy for the integrity of the medical research enterprise?

### **B. Mischaracterizing the Student Letter**

The Perez letter is a model of professional restraint and clarity. It references items that could have been checked without relying on his personality or credibility. Even so, Duke administrators sent Perez back to Nevins, a vitally interested party, without any apparent independent assessment of the information in his letter. Without knowing more, this action seems to violate several common-sense, foundational principles of institutional checks and balances.

By now, in our post-Watergate society, we should all understand that even the appearance of a cover-up is enough to provoke interest. While the lessons of painful experience do not come intuitively to investigators whose work is challenged, institutional officials should understand—and be able to convey persuasively—the reality that the moment at which credible questions surface about the validity of work is the *precise* time to seek an outside perspective, not to circle the wagons.

An integrity mindset recognizes that if the concerns are valid, internally-commissioned review permits questions to be addressed at the earliest possible moment, and corrected relatively quietly. If the concerns are unfounded, these actions create a record that can protect the researcher and the institution if the claims are perpetuated or disseminated.

Referring a vulnerable research student back to those on the ladder above him is not appropriate when there are very significant power differences between the parties; when the concerns, if true, have serious consequences, and when the vulnerable party has already made attempts to discuss the matter with those most directly affected. (8) All three of those conditions were met in the questions raised by Perez, the more so since his correspondence makes it manifestly clear that he tried to raise his concerns directly with Potti and had been rebuffed.

The question in this situation shouldn't have been “why doesn't this med student get it?” The question should have been “what if he is right” or, perhaps, “how do we make sure he is not right?”

The harm from getting the most central questions wrong about Duke's obligations to themselves, their patients, and their students was compounded by classic

elements present in other institutional failures to sustain research integrity, excessive deference to powerful researchers, and conflicts of interest.

### **2. Too Much Deference**

Duke administrators told the IOM panel that there was perhaps too much deference to “[esteemed](#)” (p. 122) and trusted faculty members.

This is not new in trials overseen by the National Cancer Institute. It is not new in cases of research misconduct. It is especially prevalent in cases not revealed until long after serious damage has been done because institutional officials are reticent about ruffling the feathers of prominent scholars.

As early as 1994, Samuel Broder, NCI director at the time, testified before Congress about the institute's failure to act on deviations from the approved enrollment protocol in breast cancer trials. These deviations were ultimately revealed through newspaper reporting, not through their own staff, who had been raising concerns for years. Broder diagnosed the cause [as follows](#): “I believe it is, in part, a function of [the PI's] formidable reputation... a pioneering figure who obviously knew a great deal. I believe there was an excessive level of collegiality and a higher level of tolerance than is now the case.”

One can argue about the details of what happened in that specific case—the controversy at the National Surgical Adjuvant Breast and Bowel Project. However, the behavior Broder describes here—deferring to luminaries—is far from unique to this case. We see it again and again.

Even though multiple institutions have learned this lesson the hard way, we seem to have a difficult time retaining and acting on it, especially when there's potentially a lot of money at stake. The cure is as straightforward as it is difficult: when problems arise, the focus must be shifted to the big picture, and the right questions posed to the right people with tact, finesse, and backbone.

### **3. Not Recognizing or Guarding Against Pervasive Conflicts of Interest**

The 2012 IOM report concludes that “there is evidence that some of those involved in the design, conduct, analysis, and reporting of the three clinical trials and related trials involving the gene-expression-based tests had either financial or intellectual conflicts of interest that were not disclosed... according to [one Duke official], there was a great deal of confusion within the university at this time about when a patent



and an intellectual property interest qualified as a conflict.” (p. 255-56)

Really?

By 2008, there were scores of articles in biomedicine demonstrating the profound influence of money (and potential money) on researchers, on institutions, on physicians, on results, not to mention reports, meetings about conflicts of interests, conferences, white papers, and policy guidelines. My own first publications about conflicts of interest were written in 1989, and I wasn't a trailblazer in the field. (9)

Interestingly, in 2001-02, the Association of American Medical Colleges and the Association of American Universities issued two reports on conflicts of interests in human subject research—one on individual and one on institutional conflicts. A Duke School of Medicine administrator was a member of the task force that developed them. The policies and guidance were updated in February 2008. Duke was also represented on that panel.

Duke had filed patents on the Nevins/Potti research, filmed a commercial for the institution featuring Dr. Potti, and held shares in the company founded to commercialize the work. The prospects were not just of financial return, but of significant wealth and renown. This was true for individuals throughout the university, and it was true for the institution itself. Stewards of a great institution are responsible for recognizing and guarding against conflicts of interest that might impair evenhanded assessments of facts, even those brought forward by a junior member of a research team or outsiders. There are policies, guidelines, and recommendations galore. What will it take to implement them more consistently and effectively?

Along with many other cases of mishandled research misconduct, this unfolding story illuminates the effect of systemic incentives and pressures in the world of big money research that can entice even the well-meaning away from an integrity mindset to one that, in the short-term, defers to power and fails to ask the right questions. Because humans are fallible, it behooves the institutions in which they work to build checks and balances, and structures that can take a longer view and ask the right questions at the right times.

### Final Thoughts

Academic research operates on trust. It is critical to be able to trust what's in the published literature. As the Nobel Laureate Joshua Lederberg put it, “above all, a publication is inscription under oath, a testimony.” (10) The authors on the byline are directly responsible

to the readers. Potti had a great number of co-authors. How is it that none of them saw the problems that were obvious to Baggerly, Coombes, and Perez?

Ironically, because the Institute of Medicine review committee was informed that Duke had contacted all 162 collaborators who were co-authors on all 40 papers by Anil Potti, and “in no instance did anyone make any inquiries or call for retractions until contacted by Duke,” the IOM committee [concluded](#) that “This experience suggests the need for co-authors to have more shared responsibility for the integrity of the published research.” (p. 251)

Too bad they didn't hear about the one person who saw such significant problems with the work that he asked for his name to be withdrawn: the medical student who took his authorship obligations so seriously that he set his own career back in order to honor them.

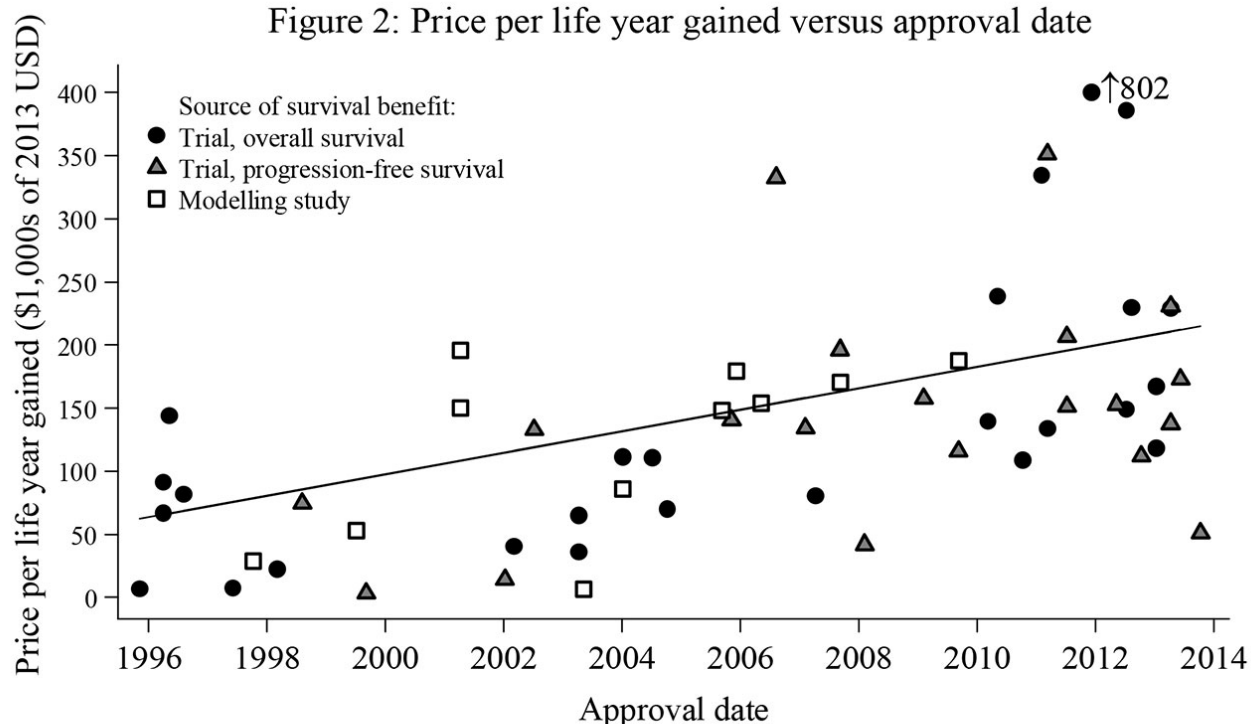
*The author is director of the National Center for Professional and Research Ethics [www.nationalethicscenter.org](http://www.nationalethicscenter.org), research professor, Coordinated Science Laboratory, professor emerita, College of Business at the University of Illinois at Urbana-Champaign. She runs [a consulting company](#) and is the author of [The Young Professional's Survival Guide](#) (Harvard University Press, 2012) and [The College Administrator's Survival Guide](#) (Harvard University Press, 2006).*

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### Endnotes:

- 1.) Unless otherwise noted, information is from documents and reporting published in The Cancer Letter.
- 2.) Gunsalus, C. K. and Drummond Rennie, “Scientific Misconduct: New Definition, Procedures, and Office—Perhaps a New Leaf.” Journal of the American Medical Association, Vol. 269, No. 7, February 17, 1993.
- 3.) Gunsalus, C. K. “Institutional Structure to Ensure Research Integrity.” Academic Medicine, Vol. 68, No. 9, September Supplement 1993.
- 4.) Alberts, et. al. PNAS paper: <http://www.pnas.org/content/111/16/5773.abstract>
- 5.) Max Bazerman, The Power of Noticing: What the Best Leaders See. Simon and Schuster 2014. New York.

Figure 2: Price per life year gained versus approval date



The best fit line is: Price per life year gained = \$54,100 + \$8,500 x Approval year.  
Approval Year = 0 for 1995, 1 for 1996, etc. For purposes of display, we re-coded one value from \$802,000 to \$400,000.

6.) This and succeeding quotes from Motions for a Summary Judgment, filed in Aiken et al. vs. Duke University et al., filed in Durham County, NC, Superior Court, [posted by The Cancer Letter, Jan. 23, 2015](#) (Walter Jacobs testimony in depositions, quoted in plaintiff memo in summary judgment motions. 12.12.14, page 10.

7.) All quotes from Motions for a Summary Judgment, filed in Aiken et al. vs. Duke University et al., filed in Durham County, N.C., Superior Court, posted by [The Cancer Letter, Jan. 23, 2015](#).

8.) See Gunsalus papers: [How to Prevent the Need for Whistleblowing: Practical Advice for University Administrators](#); [How to Blow the Whistle and Still Have a Career Afterwards](#)

9.) Gunsalus, C. K. and Rowan, Judith. "Conflict of Interest in the University Setting: I Know It When I See It." *Journal of the National Council of University Research Administrators*, Fall 1989.

10.) Lederberg, J. (1991) *Communication as the Root of Scientific Progress* (presentation at 1991 Woods Hole Conference of International Scientific Editors). Stefik, M. eds. (1993) *Internet Dreams: Archetypes, Myths and Metaphors*, 41 MIT Press Cambridge.

## Cancer Drug Prices Increased \$8,500 Per Year Since 1995

By Matthew Bin Han Ong

The launch prices of anticancer drugs have increased substantially over time—even when adjusted for inflation and survival benefits—according to a study published by the National Bureau of Economic Research.

The paper, titled "Pricing in the Market for Anticancer Drugs," was authored by David Howard, an associate professor of health policy and management at Emory University; Peter Bach, a pulmonologist and health systems researcher at Memorial Sloan Kettering Cancer Center; Ernst Berndt, the Louis E. Seley Professor in applied economics at the MIT Sloan School of Management; and Rena Conti, an assistant professor of health policy and economics at the University of Chicago.

Drug manufacturers have a temporary monopoly over drug pricing, since most drugs are on patent when FDA approves them.

"They have wide leeway, though not unlimited power, to set prices," the authors wrote.

[The study](#), published this month, evaluated pricing trends for 58 anticancer drugs approved in the U.S.

between 1995 and 2013—drugs designed to extend survival for cancer patients, with survival benefits having been estimated in trials or modeling studies.

The authors found that the drugs' average benefit- and inflation-adjusted launch prices increased by 10 percent annually, an average of \$8,500 per year, from 1995 to 2013.

"The market for anticancer drugs is economically significant," the authors wrote. "Within the market for pharmaceuticals, anticancer drugs rank first in terms of global spending by therapeutic class: \$91 billion in 2013, up from \$71 billion in 2008. The U.S. market size was \$37 billion in 2013, of which one-third was spent on 10 patent-protected cancer drugs alone.

"The market is also politically salient. Anticancer drugs figure prominently in discussions over health reform, alternately symbolizing wasteful spending and biomedical progress."

The study also found that patients and insurers are paying more over time for the same survival benefits—in quantifiable terms, the price for each year of life gained.

The price for a year of life in 1995 was \$54,100, according to the study. That number increased to \$139,100 in 2005; and to \$207,000 in 2013. These upward trends are apparent for most disease types, the authors said.

The authors offer two principal explanations for these pricing trends: reference pricing, and the growth of price discount programs.

There are strong financial incentives for physicians and hospitals to use novel products, and generous third-party coverage that insulates patients from drug prices, the authors wrote.

"We argue that under these conditions, manufacturers are able to set the prices of new products at or slightly above the prices of existing therapies, giving rise to an upward trend in launch prices," the authors wrote.

The 340B drug pricing program, authorized by Congress in 1992, has also significantly expanded, presenting manufacturers with an incentive to set higher launch prices to offset discounts (The Cancer Letter, [May 16](#), [Oct. 10, 2014](#)).

U.S. payers and providers are unlikely to change policies that fundamentally govern pricing dynamics, the authors said.

"To critics, the pricing of new anticancer drugs represents the worst excesses of a system that provides few checks on drug companies' pricing power and prioritizes gains in health, however small, over cost control," the authors wrote.

"The pessimistic view is that current coverage, reimbursement, and patent policies divert drug manufacturers' attention away from developing drugs that yield truly meaningful survival benefits.

"If insurers restricted coverage to drugs that improved survival time by an economically significant amount, perhaps there would be more of them."

## *State of the Union 2015* **President Obama Launches Precision Medicine Initiative**

*By Conor Hale*

President Barack Obama called for innovation in genetic medicine, through the launch of a new initiative, in his State of the Union address Jan. 20.

"Twenty-first century businesses will rely on American science and technology; research and development," Obama said.

"I want the country that eliminated polio and mapped the human genome to lead a new era of medicine—one that delivers the right treatment at the right time. In some patients with cystic fibrosis, this approach has reversed a disease once thought unstoppable," he said.

"So tonight, I'm launching a new precision medicine initiative, to bring us closer to curing diseases like cancer and diabetes, and to give all of us access to the personalized information we need to keep ourselves and our families healthy."

His speech referenced a guest of First Lady Michelle Obama, William Elder Jr., who was diagnosed with cystic fibrosis when he was eight years old. Following a treatment regimen focused on his own genetic mutation, Elder is now 27 years old and a third-year medical student.

"In his State of the Union address, President Obama highlighted the important role of research and innovation in growing a more prosperous and healthier nation," said Research!America President and CEO Mary Woolley. "We're pleased with the launch of the new Precision Medicine Initiative which comes at a time when the opportunity to combat disease has never been greater.

In his speech, Obama said the rate of U.S. healthcare inflation is at a 50-year low, and called for continued funding of federal research.

"A further reason, noted by the President, that we need robust funding and policies to ensure we're not behind the eight ball addressing domestic or global outbreaks like Ebola," Woolley said in a statement

following the president's address. "Current funding levels for federal health agencies put researchers at an extreme disadvantage in pursuing studies that have the potential to cure disease and improve quality of life, and tax policies have stymied the development of new drugs.

"Policymakers must pivot from short-sighted thinking to formulating a long-term strategy that will bring new treatments across the finish line and spur growth in quality jobs," she said. "We think it's past time to adopt a national strategy that will assure the U.S. retains its world leadership in science and innovation."

Currently, there are few details available about the proposed initiative. Statements from the White House have said that it may include additional funding. More information is expected in the coming weeks.

The Personalized Medicine Coalition issued a statement in support of the announcement, saying: "We look forward to learning the details, and hope that the President's plan includes needed federal policies that support personalized medicine—outlining a clear regulatory path, supporting payment policies that recognize the importance of value, and putting in place incentives for product development."

Obama also drew attention to another guest of the first lady, CVS Health President and CEO Larry Merlo, and mentioned the company's offers of education benefits and paid apprenticeships. In September 2014, CVS was one of the largest U.S. retailers to go tobacco free, halting the sale of cigarettes at its 7,700 locations.

"CVS Health set an historic example last fall when it stopped selling tobacco products in all of its stores," said Christopher Hansen, president of the American Cancer Society Cancer Action Network.

"The administration's decision to highlight one of the growing number of companies doing its part to reduce tobacco use signals tobacco control is a top national priority," Hansen said. "Elected officials and policymakers must do their part by supporting proven policies that restrict access to tobacco products, fully fund tobacco prevention and cessation programs and limit the places that people smoke."

"A critical first step is for the Food and Drug Administration to finalize its proposal to regulate all unregulated tobacco products including cigars, e-cigarettes and hookah. In addition, Congress should act quickly to build on efforts to turn the tide of tobacco addiction and increase the federal tobacco tax. If smoking persists at its current rate among youth in this country, 5.6 million Americans younger than 18 years old alive today will die prematurely from a smoking-related illness."

## ASCO Teams with SAP For CancerLinQ Project

*By Matthew Bin Han Ong*

The American Society of Clinical Oncology announced Jan. 21 that its CancerLinQ health information technology project will use the SAP HANA platform.

SAP HANA is a flexible, in-memory data management and application platform that provides predictive text analytics, spatial processing and data virtualization. SAP has teamed with medical organizations in Germany and Japan for cancer data analytics and genomic analysis.

According to ASCO, CancerLinQ is one of the only major cancer data initiatives being developed and led by physicians with the primary purpose of improving patient care.

"In teaming with SAP, we found an ideal company with state-of-the-art technology, a commitment to invest major new resources, and a clear dedication to our patient care mission," said ASCO President Peter Yu.

According to ASCO, CancerLinQ is expected to use patient care data from millions of electronic health records to provide feedback and clinical decision support to providers. Doctors should be able to receive personalized insights and help patients access care based on up-to-date findings.

Eight oncology practices around the U.S. have signed agreements with CancerLinQ to provide patient records for the first version of CancerLinQ, scheduled for release in late 2015. Seven more large cancer centers are expected to join the effort, meaning approximately 500,000 patients will be represented in CancerLinQ.

The eight oncology practices are: Inova Comprehensive Cancer & Research Institute; South Coast Centers for Cancer Care; New England Cancer Specialists; Medical Oncology Hematology Consultants PA; Cancer Treatment Centers of America; Marin Cancer Care; Space Coast Cancer Center; and Michiana Hematology-Oncology P.C.

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*Letter to the Editor*

## **Is \$100M in Stock Enough to Make MD Anderson Go Public with its Conflict-of-Interest Management Plan?**

*By Leonard Zwelling*

Last week, it was reported in both The Cancer Letter and the Houston Chronicle that The University of Texas MD Anderson Cancer Center had closed a deal to sublicense intellectual property to two pharmaceutical firms, Intrexon and Ziopharm Oncology. There is nothing terribly unusual about that.

The deals, however, were mostly in exchange for equity, \$50 million in stock from each company plus \$15-20 million per annum. The technology is chimeric antigen receptor T cells (CAR T) and The Cancer Letter article suggests that the clinical trials testing the technology's efficacy will be done at MD Anderson, at least in part.

This struck me as odd.

In 2002, after the previous President of MD Anderson was accused of conflict-of-interest on the front page of the Washington Post when 195 patients who were human subjects on clinical trials at Anderson using the drug he invented, were reported not to have known of his financial interest in their well-being following the trial, that President formed a committee to rewrite the conflict-of-interest rules for MD Anderson faculty and institutional decision makers. I was part of that committee, but it had been a long while since I had reviewed the policy and wondered if the new policy (dated 2/21/2014, Version 61.0) would allow such a deal as the newly signed one because the policy I helped author would not have allowed this stock deal to go through with trials to be run at Anderson by Anderson faculty under the President's supervision.

Here is what I found in the most recent policy:

1.) The purpose of the policy (CONFLICT OF INTEREST POLICY FOR FACULTY MEMBERS, TRAINEES, FACULTY SUPERVISORS, INSTITUTIONAL DECISION MAKERS, AND INVESTIGATORS OF THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER, #ACA0001) is still "to protect patient safety and welfare, safeguard the reputation of the institution, preserve the integrity of the affiliated research..."

2.) Compensation is defined as "any form of benefit including, but not limited to, salary, retainer,

honoraria, intellectual property rights or royalties or promised, deferred or contingent interest."

3.) Conflict of interest is defined as "a significant financial interest or outside relationship that could directly and significantly influence (or be perceived to directly and significantly influence) the employee's performance of the employee's Institutional Responsibilities, including patient care or the design, conduct, and/or reporting of research."

4.) Financial interest is defined as "anything of monetary value, whether or not the value is readily ascertainable."

5.) Institutional decision makers include the President, Executive Vice Presidents, Vice President and Chief Financial Officer, Controller and any written designees."

6.) A management plan is a "formal written plan to address a financial conflict of interest."

7.) An ownership interest is "in any corporation, partnership, or other legal entity including stock... held in blind trusts (to the extent that the identity of the companies in the portfolio in the blind trust is unknown)."

8.) A supporting entity is one "that sponsors an IRB Approved Protocol or other research study; or provides funds for a research study"

9.) Section 1.2.E prohibits making "personal investments that could reasonably create a substantial conflict between the employee's private interest and the interest of the institution;"

10.) Section 2.2.A "No research will be conducted at MD Anderson for which payment is dependent upon a specific outcome" (but wouldn't the stock value of both companies increase markedly if the clinical trials at Anderson are successful or apparently beneficial?)

11.) Section 2.2.B No Institutional Decision Maker or his/her spouse and/or dependent children may hold any Ownership Interest or receive Cash of \$10,000 or more in any 12-month period from a Supporting Entity funding research for which an MD Anderson faculty member or others at MD Anderson serve as Principal Investigator."

12.) Section 2.4.B "A Covered Individual may not serve as the Principal Investigator (or Co-Principal Investigator) for an IRB Approved Protocol or sponsored research agreement if he/she...has any Ownership Interest in the Supporting Entity...of \$10,000 or greater"

13.) Now here's the loop hole: Section 2.4.E "the President may give written permission to a faculty member with a potential Financial Conflict of Interest

authorizing that faculty member to act as the Principal Investigator of that IRB Approved Protocol.” (In other word, numbers 1 through 12 no longer matter if the President says they don’t.)

14.) However, in such a case, if the investigator “holds equity in the Supporting Entity, the IRB Approved Clinical Protocol must be multi-institutional, and the lead Principal Investigator must be an individual from another institution.”

15.) “Neither faculty members nor the institution may hold the Investigational New Drug Application (IND) for such an IRB Approved Protocol.”

16.) Section 9.3 “No direct Supervisor will be responsible for oversight or approval of another person’s compliance with the commitment of time requirements as specified...if such Supervisor has an Ownership Interest...from the outside entity...”

17.) In section 10.1 it states “if MD Anderson has an Ownership Interest in a Supporting Entity funding, any IRB Approved Protocols related to that Supporting Entity, such IRB Approved Protocols will be reviewed at least once a year by an independent clinical research monitoring organization, which will review all efficacy and safety data, and this relationship will be disclosed on the patient informed consent documents. Phase I and Phase II IND exempt studies may be conducted entirely within the institution; Phase II studies must be conducted as multi-institutional trials; Phase III studies and Phase II studies aimed at gaining FDA approval... must be conducted as multi-institutional trials with the lead Principal Investigator being from an institution other than MD Anderson.”

18.) In section 12.1 on Compliance the reporting of non-compliance is to the very Institutional Decision Makers referred to as being covered by the policy.

So all I am asking is that MD Anderson reveal the details of the new agreements.

1.) Who owns the \$100M in stock? It surely cannot be in a blind trust. We all know what’s in it.

2.) Who is overseeing whom when the trials start?

3.) Where will the CAR T cells be manufactured?

4.) Where will the trials be done and who are the lead investigators and do they have any of this stock themselves?

5.) Why did they bother writing a policy when the President can wave a wand and excuse all the bad behavior the policy putatively outlaws?

6.) And what is going to prevent Dr. DePinho from asking for another appearance on CNBC to push these two stocks as he pushed Aveo before that company imploded? (Look at what happened just

because of the MD Anderson announcement):

From the New York Times’ Andrew Pollock, January 19, 2015:

“Last week, two companies working together agreed to pay the MD Anderson Cancer Center \$100 million in stock for technology that can be used in such therapy. They paid an additional \$15 million in stock to persuade the cancer center to sign the deal in time for it to be announced at the J.P. Morgan conference.”

“Expensive as that was as a public relations strategy, it paid off, at least in the short run. Shares of one of the companies, Ziopharm Oncology, went up 55 percent on Wednesday, the day after the announcement was made. Shares of the other, Intrexon, rose 31 percent.”

What am I missing?

How can this arrangement as announced possibly be in compliance with the latest COI policy of MD Anderson and if so, let’s see the details.

*Zwelling is a medical oncologist and former vice president for research administration at MD Anderson.*

## **MD’s Anderson’s Responds: Consider the Source and Venue**

*This letter from the MD Anderson administration and received from Jim Newman, director for external communications.*

To The Cancer Letter:

Throughout the past three years, The Cancer Letter seems to have been willing to print whatever allegations were provided to it concerning MD Anderson, with seemingly no effort to determine the credibility of the sources or legitimacy of the accusations.

While our responses to several of the publication’s assertions have attempted to provide a more factual picture, we have not previously gone on record to question the bias of sources or slanted commentary presented, as we have been confident that the readership is aware of the great work done by our 20,000 cancer fighting people every day.

Following The Cancer Letter’s invitation to respond to the latest criticism from a former faculty member who failed to obtain peer-reviewed support for reappointment, was faced with the reality of no longer being employed at MD Anderson, and subsequently left the institution for another position from which he was terminated within months, we believe the time has come to make the record factually accurate.

Dr. Zwelling's lengthy criticism of MD Anderson's license agreement with two biotechnology companies, which will enable further development of CAR T therapies, is nothing more than highly selective and misleading quotes from MD Anderson's Conflict of Interest Policy coupled with a list of questions based on his own fictional hypotheticals.

Here's what readers need to know:

The agreement announced last week does not in any way violate MD Anderson's Conflict of Interest Policy, which is comparable to policies at other fine academic institutions. We invite your audience to read the policy themselves <http://www.mdanderson.org/about-us/compliance-program/handbook-of-operating-procedures/aca0001.pdf>. As one who claims to have been a partial author of previous versions of the policy, we are surprised Dr. Zwelling does not recognize that the agreement can be successfully managed in accordance with both the current policy, as well as previous versions.

The reality of the situation is this: While MD Anderson is currently conducting a handful of CAR T therapy studies, no one who will personally benefit from the agreement is directing those active studies, nor will they be allowed to do so in the future. Furthermore, those who will personally benefit are the exceptional scientists and doctors who have produced this outstanding work. Most academic institutions actively promote such efforts through rules that provide for sharing licensing benefits with inventors. Moreover, there are no current studies at MD Anderson being funded by either of the companies who licensed the technology. MD Anderson's Conflict of Interest Committee and other responsible offices will nevertheless monitor the situation to ensure if and when potential conflicts arise, they will be addressed quickly and appropriately.

If and when one or more of the MD Anderson investigators who pioneered this approach do apply to conduct new CAR T trials, we will do what we always do—review the situation and determine if (a) a conflict of interest exists, and if so (b) whether the conflict is best eliminated or managed. If the conflict can be appropriately managed, MD Anderson will then create a customized conflict of interest plan with impartial oversight so that the research follows institutional guidelines created to ensure patient care decisions are not impacted and research is conducted without bias. Our position on these matters remains the same—patient safety comes first and research integrity is just as important. This has been the case for 74 years

and it will continue for generations to come. On both individual and institutional conflict issues, there are multiple ways that a conflict can be managed, all with necessary monitoring and transparency. Guidelines for managing conflicts have always been a part of our rules.

Given MD Anderson's current strong, stable financial position, the value from the transaction ultimately received by the institution after it is shared with another university, inventors and potentially other entities, coupled with the conflict management safeguards that will undoubtedly be taken if required, demonstrates the absurdity of suggesting that the institutional holding in these shares could even remotely influence the work done by our world-class faculty. Moreover, it is our solemn responsibility to save lives by converting discoveries in journals to medicines in the clinic through a number of mechanisms including collaborations with the private sector. If such life-saving collaborations yield a monetary return for the institution, those resources are reinvested in our mission areas of patient care, prevention, research and education.

Dr. Zwelling decries the fact that a portion of MD Anderson's Conflict of Interest Policy can be adapted in special circumstances. He selectively quotes the policy when making this point. A quick review of it reveals that Dr. Zwelling's broad claim that the policy allows the president to "excuse all bad behavior" is highly-inaccurate at best and highly manipulative at worst.

In closing, while Dr. Zwelling publicly shares his disgruntled criticisms of his former employer on a near-daily basis through various venues, in this case it appears his frustrations with MD Anderson have clouded both his memory and judgment. We feel his most recent comments to *The Cancer Letter* are unfair to both his former colleagues and other caring people who continue to fight this disease every day through exceptional clinical care and decisive research with the potential of bringing new medicines to suffering patients and their families.

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Letter to the Editor

## LLS President Responds To "Bad Luck" Cancer Study

By Louis J. DeGennaro

A [new study](#) indicates that the risk of developing cancer in some types of tissue is based on the frequency of stem cell divisions, and therefore beyond individuals' control to minimize their own risks. As the study stated, a majority of these cancers develop due to random mutations of noncancerous stem cells; in other words, it's just "bad luck."

This pessimistic conclusion may cause cynicism or a feeling of hopelessness. In a recent, controversial move, [a top medical voice](#) in the U.K. declared we should "stop wasting billions trying to cure cancer." This statement was met with great public outcry. And, rightly so, because at this very moment there is cause for great hope in the field of cancer treatment.

I saw evidence [at last month's meeting of the American Society of Hematology](#), where a number of breakthroughs were presented for the treatment of blood cancers, including leukemia, lymphoma, myeloma and myelodysplastic syndromes. I have never come away from a medical meeting as excited as I was after this meeting, to see the full potential of those breakthroughs and the therapies and discoveries that are in the pipeline, which, in my lifetime, have never been so plentiful. In my estimation, we will see a constant stream of new therapies to treat blood cancers because of the research investment being made by world-class researchers, hospitals, biopharmaceutical companies, and patient advocacy organizations like the Leukemia & Lymphoma Society.

What is the role of LLS and similar organizations in the search to find new cancer treatments? They have several parts to play in the quest for treating and curing cancers. By leveraging our research funding and advocacy network, LLS is able to bring together all of the players in the ecosystem of the delivery of new therapies to patients. We facilitate collaboration among:

- Academic researchers and physician scientists. They make the early discoveries.
- Pharmaceutical and biotechnology industries. They translate those knowledge breakthroughs into potential therapies for patients and conduct clinical trials.
- Regulatory agencies, including the FDA, who evaluate the safety and efficacy of new therapies for patients.
- Payers, both public and private, such as the insurance industry and publicly funded programs like

Medicare or Medicaid, which help patients get access to therapies.

- Patients and their doctors, who make critical decisions about which therapies are appropriate

Organizations like the LLS are in a unique position to bring together all of those players in the ecosystem to help accelerate new therapies to patients and to ensure patients have access to the lifesaving treatments they desperately need. We provide free disease information, professional education, co-pay assistance and other patient support programs through our national office as well as our chapters across the U.S. and Canada. We are a strong voice in Washington, D.C., and throughout the U.S., representing the healthcare and medical research interests of patients and families to policy makers at all levels of government.

Though our research programs are focused on blood cancer therapies, time and again investigators report that therapies pioneered in the blood cancers show very remarkable results in other cancers, as well. For example, among the highlights of the American Society of Hematology meeting last December were advances in immunotherapy. Pioneered in the blood cancers, immunotherapy approaches are now being studied for treating patients with breast cancer, pancreatic cancer and ovarian cancer. In other words, blood cancer research is paving the superhighway to other cancer cures. At LLS, we are making an investment in blood cancer research, and we are seeing therapies that are demonstrating great potential for blood cancer patients as well as for patients with other cancers and other serious diseases. For example, there's a blood cancer treatment, originally developed for lymphoma, which is now being used to treat rheumatoid arthritis. There is significant current progress, tremendous hope for the future and lifesaving impact across multiple cancers and even into other diseases.

So we have to keep up the pressure. We have to continue to be strategic. We have to continue to be effective in our funding, in order to continue to drive those near-term therapies to patients.

*DeGennaro is the president and chief executive officer of The Leukemia & Lymphoma Society. LLS is the world's largest voluntary health agency dedicated to curing blood cancer patients.*

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### *In Brief*

## **Lancaster Leaves Moffitt To Join Myriad Genetics**

**JOHNATHAN LANCASTER** joined **Myriad Genetics** as vice president of medical affairs for oncology in Myriad Genetic Laboratories, effective Feb. 9.

Lancaster will provide medical and scientific leadership across Myriad's expanding portfolio of molecular and companion diagnostic products and services for oncology.

Over the past 12 years, he held leadership positions at Moffitt Cancer Center, including president of Moffitt Medical Group, deputy physician-in-chief, director of the Center for Women's Oncology, and chair of the Department of Women's Oncology. Before Moffitt, Lancaster was a medical director of the Gynecologic Dysplasia Clinic at Duke University Medical Center, where he also completed his residency and fellowship training.

**SUE BIGGINS** was awarded the Edward Novitski Prize by the **Genetics Society of America**.

Biggins is a researcher at Fred Hutchinson Cancer Research Center. The award recognizes her research on the molecular mechanisms of chromosome segregation, a process essential for cell division and frequently impaired in cancer.

Biggins has been studying the kinetochore, a molecular machine that mediates chromosome segregation during cell division, for the last 20 years. Before her work, kinetochores had been challenging to isolate and investigate due to their complex, dynamic nature. Biggins tackled this problem in the budding yeast *Saccharomyces cerevisiae*, in which the chromosome segregation machinery is a simplified version of that found in humans. She accomplished the first isolation of the kinetochore in any organism by developing an elegant one-step method.

Biggins has been a GSA member for 15 years, is an associate editor of the society's flagship journal *Genetics*, and has served on the organizing committee of GSA's biannual Yeast Genetics Meeting since 2010. She also belongs to the American Society for Cell Biology, where she recently served as an elected council member. In 2013, she received the National Academy of Sciences Award in Molecular Biology for her work on kinetochores and the McDougall Mentoring Award from the Fred Hutchinson Cancer Research Center.

**THE PANCREATIC CANCER ACTION NETWORK** and NCI's **Frederick National Laboratory for Cancer Research** will award two fellowships to support research on KRAS mutations that are relevant to pancreatic cancer.

The recipients are **John Hunter**, of the University of Texas Southwestern Medical Center, and **Lynn McGregor**, of the University of California, San Francisco.

In addition to receiving financial support for their research, Hunter and McGregor will receive training and mentorship by the RAS team at FNLCR. They also will be involved in the network's Community for Progress and have opportunities to participate in scientific meetings, establish research collaborations, and engage with the broader pancreatic cancer community.

**CARIS LIFE SCIENCES** established the **Caris Centers of Excellence for Precision Medicine Network**, appointing **John Marshall** as chairman.

Marshall is professor of medicine and oncology at Georgetown University School of Medicine, and chief of hematology/oncology at Georgetown Lombardi Comprehensive Cancer Center/MedStar Georgetown University Hospital.

The network will consist of cancer centers working collaboratively to advance the delivery of tumor profiling and establish standards of care for molecular profiling in oncology. As chairman of the network, Marshall will lead the development of guidelines and standards for tumor profiling, draft research protocols using tumor profiling to help guide therapy decisions, and establish a collaborative forum for sharing best-practices, profiling implementation strategies and case evaluations for network members.

In addition, the network will provide a platform to promote research initiatives utilizing tumor profiling and data mining of the Caris Life Sciences' database of more than 68,000 patient profiles, including outcomes data from over 2,400 patients that have been tracked over a five-year period.

**CITY OF HOPE** and **Trovagene Inc.** entered into a clinical collaboration to conduct studies on detecting and monitoring EGFR mutations in lung cancer patients using Trovagene's Precision Cancer Monitoring platform.

The clinical study is expected to enroll 75 patients with lung cancer. Primary objectives of the study include evaluating concordance between urinary circulating tumor DNA, blood ctDNA, and tumor tissue

for determining EGFR mutational status.

Additionally, the study investigators will evaluate the quantitative and qualitative performance of longitudinal EGFR mutation monitoring using both urine and blood specimens, as they relate to response to therapy over time. Exploratory objectives include evaluating the feasibility of identifying the TKI-resistant mutation, T790M, in urinary and blood ctDNA at the time of progression.

**WuXi PharmaTech (Cayman) Inc.** acquired **NextCODE Health** for \$65 million in cash, with plans to merge NextCODE and WuXi's Genome Center into a new company, named WuXi NextCODE Genomics.

The business will be headquartered in Shanghai, with operations in Cambridge, Mass., and Reykjavik. The leadership of WuXi NextCODE Genomics will include Ge Li as CEO, Edward Hu as CFO, Hannes Smarason as COO, Jeffrey Gulcher as CSO, Hongye Sun as CTO, and Hakon Gudbjartsson as VP of Informatics.

NextCODE Health was spun out from deCODE genetics after the latter was acquired by Amgen in December 2012. In October 2013, NextCODE Health announced that it had obtained from Amgen a five-year exclusive license for sequence-based clinical diagnostic applications using technology developed by deCODE genetics.

**THE MEDICAL UNIVERSITY OF SOUTH CAROLINA Hollings Cancer Center's** Mount Pleasant location installed TrueBeam imaging capabilities for patients, as well as several types of external beam radiation therapy.

The addition of TrueBeam technology at Hollings Cancer Center/Mt. Pleasant is the latest in a series of technology upgrades made across MUSC Health's radiation oncology program over the past few months. A similar TrueBeam system was installed at the main Charleston location in August 2014, while a major upgrade of the Gamma Knife Center's stereotactic radiosurgery system was completed in September 2014.

A public open house event will be held Feb. 12 at Hollings Cancer Center/Mt. Pleasant, featuring demonstrations of the new system.

**ROYAL PHILIPS** will analyze pathology samples using advanced image analysis algorithms from **Indica Labs Inc.** as part of its Digital Pathology Solutions offerings.

The collaboration will allow pathology researchers to apply algorithms to digitized pathology slides, which

may enhance their ability to detect, process and extract information from tissue samples than currently possible using a conventional microscope. The collaboration will combine the Philips Digital Pathology Solution and Indica's HALO image analysis platform.

**PICADOR** acquired world rights to a debut novel by **Paul Goldberg**, editor and publisher of *The Cancer Letter*. Set in Moscow in late February and early March of 1953, the novel is only in part about medicine. It's expected to be published in early 2016.

Publishers Weekly [ran this announcement](#) of the deal:

In his first acquisition after over a decade in the industry, James Meader, executive v-p of publicity at Picador, preempted world rights to Paul Goldberg's debut novel, *The Yid*.

Josh Getzler at Hannigan Salky Getzler represented Goldberg, the longtime editor of *The Cancer Letter*, an online weekly that shares information on, among other things, new treatments and research.

The novel, Meader said, is "darkly comic" and was pitched as "Inglorious Bastards crossed with Seven Samurai, with echoes of Shakespeare, Yiddish humor, and tragicomedy." *The Yid* follows a group of intellectuals in Moscow in 1953—among them an actor, a doctor, and an African-American living in Moscow—who hatch a plot to assassinate Stalin."

## Drugs and Targets **CHMP Grants Positive Opinion To Jakavi in Polycythemia Vera**

**The Committee for Medicinal Products for Human Use** of the European Medicines Agency adopted a positive opinion for **Jakavi (ruxolitinib)** for the treatment of adult patients with polycythemia vera who are resistant to or intolerant of hydroxyurea. If approved in the EU, ruxolitinib could provide the first targeted treatment option for these patients.

In PV, patients with resistance to or intolerance of hydroxyurea are considered to have uncontrolled disease, which is typically defined as hematocrit levels greater than 45 percent, elevated white blood cell count and/or platelet count, and may be accompanied by debilitating symptoms and/or enlarged spleen.

The European Commission delivers its final decision within three months of the CHMP recommendation. The decision will be applicable to all 28 EU member states plus Iceland, Norway and Liechtenstein. Global regulatory applications for ruxolitinib in PV are currently ongoing, and

further regulatory filings are under review by health authorities. Ruxolitinib, which is marketed in the U.S. by Incyte Corporation as Jakafi, received approval in December 2014 from FDA for the treatment of patients with PV who have had an inadequate response to or are intolerant of hydroxyurea.

The CHMP recommendation was based on results from the phase III RESPONSE clinical trial demonstrating that a significantly greater proportion of patients achieved the composite primary endpoint of hematocrit control (volume percentage of red blood cells in whole blood) without use of phlebotomy (a procedure to remove blood from the body to reduce the concentration of red blood cells) and spleen size reduction when treated with ruxolitinib compared to best available therapy (21 percent compared to 1 percent, respectively;  $p < 0.0001$ ).

In addition, a greater proportion of patients in the ruxolitinib treatment arm achieved complete hematologic remission, as defined by the modified 2009 European LeukemiaNet criteria, when compared to the standard therapy arm (24 percent compared to 9 percent, respectively;  $p = 0.003$ ). The data also showed more patients treated with ruxolitinib had a durable primary response at week 48 compared to patients treated with standard therapy (19 percent compared to 1 percent, respectively;  $p < 0.0001$ ).

**Palmetto GBA**, a national contractor that administers Medicare benefits, issued a positive coverage policy through the MoIDX Program for **the Decipher prostate cancer classifier** developed by GenomeDx Biosciences.

Decipher is a unique genomic test intended for men who have had prostate surgery and are considered by guidelines to be at risk for their cancer returning. These are men who have specific risk factors for

cancer recurrence, including positive surgical margins, pathological stage T3 disease (seminal vesicle invasion, extraprostatic extension, bladder neck invasion) or rising PSA after initial PSA nadir. The Medicare coverage policy covers men with prostate cancer who have these features and are weighing treatment options after a radical prostatectomy.

Clinical data generated in the development of Decipher showed improved accuracy in predicting aggressive prostate cancer, and test results impacted physicians' treatment decisions, with the potential to provide cost-savings to the healthcare system and to spare patients the burden of life-altering side effects associated with additional treatment.

In published clinical validation and utility studies, 60 percent of men classified as high risk by traditional tools were reclassified as low risk by the Decipher test and 98.5 percent of these men had no incidence of metastasis within five years of surgery. Thirty to 40 percent of the time, physicians changed their treatment recommendations based on the results of the Decipher test. Further, recent studies suggest that Decipher may predict which men will benefit from radiation therapy after surgery and which may not.

**VENTANA MEDICAL SYSTEMS INC.**, a member of the Roche Group, announced its FDA submission for premarket approval of the VENTANA ALK (D5F3) CDx Assay.

The companion diagnostic immunohistochemistry test is designed to identify ALK(1)-positive lung cancer patients that may benefit from treatment with targeted therapy that inhibits the ALK gene. This submission was the fourth and final module and application required by the FDA's premarket process.

IHC testing is widely accessible on VENTANA BenchMark XT instruments.

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